



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/555,986 | 08/17/2000 | Gregor Cevc | 500.1011 | 9461 |

7590 04/01/2005

PETER CORLESS, ESQ.
EDWARDS & ANGELL, LLP
P. O. BOX 55874
BOSTON, MA 02205

EXAMINER

KISHORE, GOLLAMUDI S

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1615

DATE MAILED: 04/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/555,986

Applicant(s)

CEVC, GREGOR

Examiner

Gollamudi S. Kishore, Ph.D

Art Unit

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 December 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 199-224 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 199-224 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The RCE dated 12-21-04 acknowledged.

Claims included in the prosecution are 199-224.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
2. Claims 199-224 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

'lipid-like materials' in the independent claims is deemed to be indefinite since it is unclear what lipids it represents. The examiner suggests reciting specific lipids.

The distinction between 'surface-active substances' and surfactants is unclear. Surfactants affect surface tension of a liquid and therefore are surface-acting substances. 'the liquid medium' in the independent claims lacks antecedent basis.

Furthermore, claims 199 and 215 as recited are very confusing. According to claim 199, the substrate is formed by combination of one surface-building lipid and one surface-destabilizing lipid, which apparently are

both amphipathic. If the surface built by one lipid is destabilized by the other lipid, then how can a substrate form by this combination and how can the third amphipathic substance bind to the substrate? What is the nature of the substrate formed. The examiner once again suggests reciting the specific components and their amounts in the independent claims.

Claim 200 recites, "the substrates are in the form of membrane surfaces". Does this mean the substrates as recited in the parent claim need not have membrane surfaces? If they do not have the membranes how can the third substance get attached to the substrate? What is the nature of the substrate?

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 199-224 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 92/03122 of record.

According to instant claim 199, the composition contains three components and the process involves,

selecting the at least one first and the at least one second substance,
combining the first and second substances in contact with the liquid medium to

form substrates,

selecting the at least one third substance,

allowing the molecules of the third substance to associate with the substrate

formed by the at least one first and the at least one second substance.

WO discloses a composition containing two or more amphiphilic substances with different solubilities for the administration of various active substances including insulin.

The first amphipathic substance is a phospholipid, the second amphipathic substance is sodium cholate and the third substance is insulin or an immunoglobulin or a hormone (note the abstract and entire publication, in particular, examples and claims of the English translation).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that instant claims require the addition of the third substance after the addition of the first and second substance whereas in WO 92, droplets are formed from a solution containing the active agent. This argument is not found to be persuasive for two reasons. WO 92 discloses several examples containing either inulin or insulin. According to example 166 (page 129 of English translation) in the reference, phosphatidylcholine (first substance) and sodium cholate (second substance) are combined in ethanol (liquid medium) to form a substrate. To this an aqueous solution of insulin is added. This step naturally associates the third substance with the substrate. In examples 163-165 (page 127 of English translation), the reference uses inulin and in this example, inulin is added to the mixture of PC and cholate. The reference thus, meets the requirements of instant claims.

Art Unit: 1615

5. Claims 199-208 and 213-220 are rejected under 35 U.S.C. 102(b) as being anticipated by Weder (4,731,210).

Weder discloses compositions containing an amphiphathic phospholipid, an amphipathic surfactant (cholic acid and salts) and an active agent, which is an antibody or a hormone (calcitonin and steroidal hormones). The phospholipids include lecithin, phosphatidic acid and others. The process involves mixing the phospholipid and the solubilizing agent (sodium cholate) and adding the antibody, which is absorbed on the surface of the liposome (abstract, col. 8, line 35 through col. 9, line 67, Examples and claims, claim 4 in particular).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 199-224 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 92/03122 cited above by itself, or in further combination with either Uster (4,944,948).

The teachings of WO have been discussed above. In essence, WO basically teaches a combination of the three amphipathic substances claimed. In the process of

Art Unit: 1615

preparation, WO teaches both methods, that is, mixing all three components together and also adding the third substance (inulin) to already formed membrane structures. Although WO does not specifically show through examples the second method as applied to insulin, interferons and other claimed molecules. It would have been obvious to one of ordinary skill in the art to use these substances as the third substance in the taught method with a reasonable expectation of success. What is unclear from WO is whether the third substance (macromolecule) is on the surface of the vesicles. Assuming that it is not, attaching a macromolecule on the surface, if that is desired, is deemed obvious to one of ordinary skill in the art since the reference of Uster teaches that when a macromolecule such as EGF can either be encapsulated or attached to the surface of the vesicles with the same release rates (abstract and col. 8, line 29 et seq., col. 10, line 61 et seq.). One of ordinary skill in the art would expect at least similar results. Uster further teaches on col. 4, lines 26-32 that the negative charge on the vesicles enables the EGF molecules to adsorb on the surface of the vesicles. Although Uster does not teach macro molecules other than EGF, WO teaches a variety of macro molecules and it would have been obvious to one of ordinary skill in the art based on Uster's statement that any macromolecule could be attached to the surface of the vesicles, if such is desired and with the expectation of obtaining at least similar results.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant's arguments once again pertain to the lack of teachings or suggestions in WO to a combination of first, second and third substances. These have been addressed above. The general arguments with regard to Uster have also been

Art Unit: 1615

addressed before Applicant argues that Uster does not describe or suggest a third amphipathic amphipathic substance. Applicant also argues that Klibanov relates to the prolongation of circulation time of liposomes and how far the substances employed for this prolongation are capable of influencing the target binding and retention of the liposomes. These arguments are not found to be persuasive since these references teach the concept of the macromolecule being at the external surface of the liposomes and the motivation to combine need not be the same as applicant's. The rejection therefore, is maintained.

8. Claims 199-224 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weder (4,731,210) by itself or in combination with WO 92/03122 cited above.

As pointed out above, Weder discloses compositions containing an amphipathic phospholipid, an amphipathic surfactant (cholic acid and salts) and an active agent, which is an antibody. The process involves mixing the phospholipid and the solubilizing agent (sodium cholate) and adding the antibody, which is absorbed on the surface of the liposome (abstract, col. 8, line 35 through col. 9, line 67, Examples and claims, claim 4 in particular). Weder does not specifically disclose claimed insulin or interleukin. However, since Weder provides guidance through examples as to how to absorb the active agent on the surface of the liposome and is suggestive of the applicability of the method to proteins, it would have been obvious to one of ordinary skill in the art to use claimed insulin or interleukin with a reasonable expectation of success. One of ordinary skill in the art would be motivated further to use these active agents since the reference

Art Unit: 1615

of WO which teaches similar compositions is suggestive of the feasibility of the use of insulin.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 199-224 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 31, 38 and 70-76 of copending Application No. 09/621,574. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims in both applications are drawn to the same compositions and the ratios of the lipid to the surfactant recited in the claims of said copending application fall within the generic terms in instant claims. The species of specific active agents recited in instant claims are deemed to be anticipated by the generic term, active agent in the claims of said copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Art Unit: 1615

3. Claims 199-224 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-66, 80-81, 88-100 of copending Application No. 10/357,618. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims in both applications are drawn to the same compositions and instant species of active substances are deemed to be anticipated by the generic active ingredient recited in the claims of said patent. 'container', 'package' in which the compositions are placed as recited in claims 80, 81 and others recited in the copending application are deemed to be obvious forms for the composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The reference of Pratap Singh (6,248,353), which teaches that protein incorporation into phospholipid-sodium cholate or lysolecithin membranes is known in the art, is cited of interest (col. 1, line 47 et seq.).

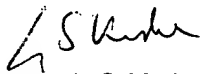
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone

Art Unit: 1615

number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK